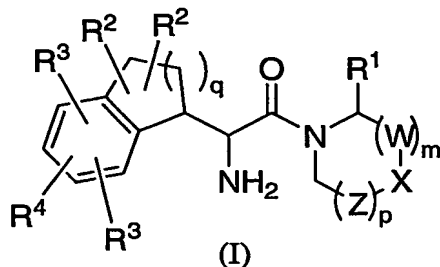


WHAT IS CLAIMED IS:

1. A compound of the formula I:



- 5 or a pharmaceutically acceptable salt thereof; wherein
 each n is independently 0, 1, or 2;
 m and p are each independently 0 or 1;
 q is 1 or 2;
- 10 X is CH₂, S, SO, SO₂, CHF, or CF₂;
 W and Z are each independently CH₂, CHF, or CF₂;
 R¹ is hydrogen or cyano;
- 15 each R² is independently selected from the group consisting of hydrogen, halogen, C₁₋₄ alkyl,
 C₁₋₄ alkoxy, trifluoromethyl, trifluoromethoxy, and hydroxy;
- each R³ is independently selected from the group consisting of hydrogen, halogen, C₁₋₄ alkyl,
 C₁₋₄ alkoxy, trifluoromethyl, trifluoromethoxy, and hydroxy;
- 20 R⁴ is hydrogen, halogen, aryl, heteroaryl, or heterocyclyl, wherein aryl, heteroaryl, and
 heterocyclyl are unsubstituted or substituted with one to five R⁵ substituents;
- each R⁵ is independently selected from the group consisting of
 halogen,
 25 cyano,
 oxo,
 hydroxy,
 C₁₋₆ alkyl, wherein alkyl is unsubstituted or substituted with one to five halogens,
 C₁₋₆ alkoxy, wherein alkoxy is unsubstituted or substituted with one to five halogens,

$(CH_2)_n-NR^6R^7$,
 $(CH_2)_n-CONR^6R^7$,
 $(CH_2)_n-OCONR^6R^7$,
 $(CH_2)_n-SO_2NR^6R^7$,
5 $(CH_2)_n-SO_2R^9$,
 $(CH_2)_n-NR^8SO_2R^9$,
 $(CH_2)_n-NR^8CONR^6R^7$,
 $(CH_2)_n-NR^8COR^8$,
 $(CH_2)_n-NR^8CO_2R^9$,
10 $(CH_2)_n-COOH$,
 $(CH_2)_n-COOC_{1-6}$ alkyl,
 $(CH_2)_n$ -aryl, wherein aryl is unsubstituted or substituted with one to five substituents
independently selected from halogen, hydroxy, CO_2H ,
C₁₋₆ alkyloxycarbonyl, C₁₋₆ alkyl, C₃₋₆ cycloalkyl, and C₁₋₆ alkoxy, wherein
15 alkyl and alkoxy are unsubstituted or substituted with one to five halogens,
 $(CH_2)_n$ -heteroaryl, wherein heteroaryl is unsubstituted or substituted with one to three
substituents independently selected from hydroxy, halogen, CO_2H , C₁₋₆
alkyloxycarbonyl, C₁₋₆ alkyl, C₃₋₆ cycloalkyl, and C₁₋₆ alkoxy, wherein alkyl
and alkoxy are unsubstituted or substituted with one to five halogens,
20 $(CH_2)_n$ -heterocyclyl, wherein heterocyclyl is unsubstituted or substituted with one to
three substituents independently selected from oxo, hydroxy, halogen, CO_2H ,
C₁₋₆ alkyloxycarbonyl, C₁₋₆ alkyl, C₃₋₆ cycloalkyl, and C₁₋₆ alkoxy, wherein
alkyl and alkoxy are unsubstituted or substituted with one to five halogens,
25 $(CH_2)_n$ -C₃₋₆ cycloalkyl, wherein cycloalkyl is unsubstituted or substituted with one to
three substituents independently selected from halogen, hydroxy, C₁₋₆ alkyl, and
C₁₋₆ alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one
to five halogens,
wherein any methylene (CH_2) carbon atom in R^5 is unsubstituted or substituted with one
to two groups independently selected from halogen, hydroxy, and C₁₋₄ alkyl
30 unsubstituted or substituted with one to five halogens;

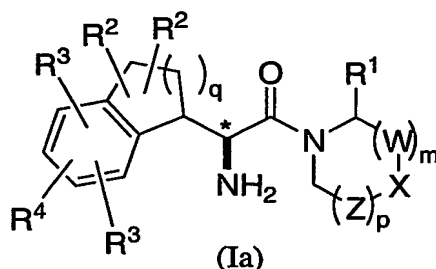
R^6 and R^7 are each independently selected from the group consisting of hydrogen, tetrazolyl,
thiazolyl, $(CH_2)_n$ -phenyl, $(CH_2)_n$ -C₃₋₆ cycloalkyl, and C₁₋₆ alkyl, wherein alkyl is
unsubstituted or substituted with one to five substituents independently selected from halogen
35 and hydroxy and wherein phenyl and cycloalkyl are unsubstituted or substituted with one to five

substituents independently selected from halogen, hydroxy, C₁₋₆ alkyl, and C₁₋₆ alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens; or R⁶ and R⁷ together with the nitrogen atom to which they are attached form a heterocyclic ring selected from azetidine, pyrrolidine, piperidine, piperazine, and morpholine wherein said
 5 heterocyclic ring is unsubstituted or substituted with one to three substituents independently selected from halogen, hydroxy, C₁₋₆ alkyl, and C₁₋₆ alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens; and

each R⁹ is independently selected from the group consisting of tetrazolyl, thiazolyl, (CH₂)_n-phenyl, (CH₂)_n-C₃₋₆ cycloalkyl, and C₁₋₆ alkyl, wherein alkyl is unsubstituted or substituted
 10 with one to five halogens and wherein phenyl and cycloalkyl are unsubstituted or substituted with one to five substituents independently selected from halogen, hydroxy, C₁₋₆ alkyl, and C₁₋₆ alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens, and wherein any methylene (CH₂) carbon atom in R⁹ is unsubstituted or substituted with one to
 15 two groups independently selected from halogen, hydroxy, and C₁₋₄ alkyl unsubstituted or substituted with one to five halogens; and

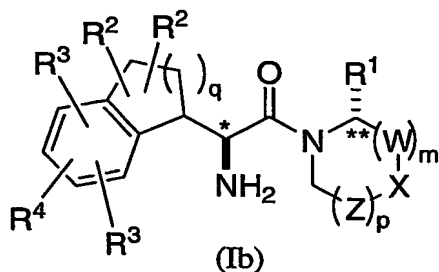
each R⁸ is hydrogen or R⁹.

20 2. The compound of Claim 1 wherein the carbon atom marked with an * has the stereochemical configuration as depicted in formula Ia:

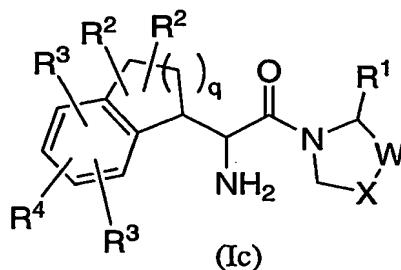


wherein R² and R³ are each independently hydrogen or fluorine; and W, X, Z, m, p, q, R¹, and R⁴ are as defined in Claim 1.

25 3. The compound of Claim 2 wherein the carbon atom marked with an ** has the stereochemical configuration as depicted in formula Ib:

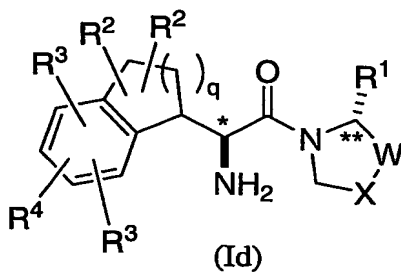


4. The compound of Claim 1 wherein m is 1 and p is 0 as depicted in formula Ic:



5 wherein R² and R³ are independently hydrogen or fluorine, and W, X, q, R¹, and R⁴ are as defined in Claim 1.

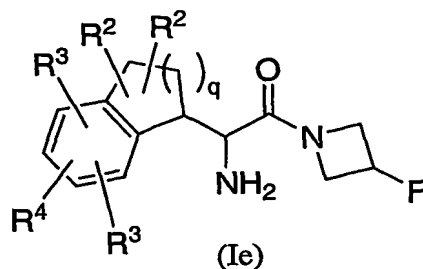
5. The compound of Claim 4 wherein the carbon atom marked with an * and the carbon atom marked with an ** have the stereochemical configurations as depicted in the formula Id:



wherein R² and R³ are each independently hydrogen or fluorine, and W, X, q, R¹, and R⁴ are as defined in Claim 1.

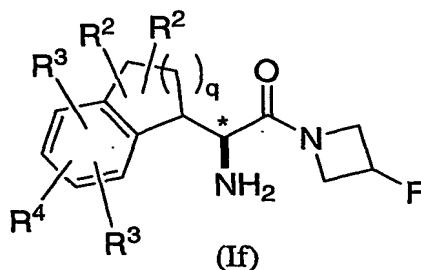
6. The compound of Claim 5 wherein R¹ is hydrogen; W is CH₂; and X is CH₂, CHF or CF₂.

7. The compound of Claim 1 wherein R^1 is hydrogen and m and p are 0 as depicted in the formula Ie:



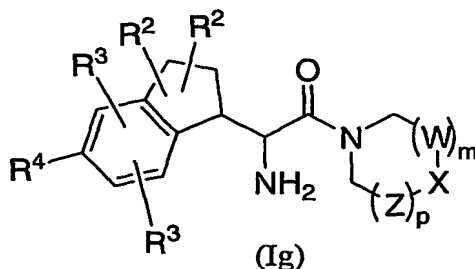
wherein R^2 and R^3 are each independently hydrogen or fluorine, and q and R^4 are as defined in Claim 1.

8. The compound of Claim 7 wherein the carbon atom marked with an * has the stereochemical configuration as depicted in the formula If:



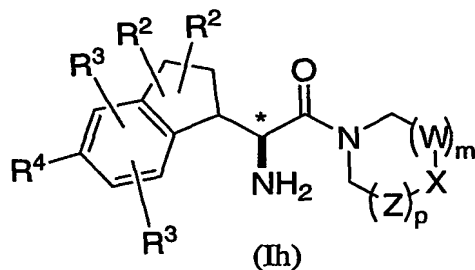
wherein R^2 and R^3 are each independently hydrogen or fluorine, and q and R^4 are as defined in Claim 1.

9. The compound of Claim 1 of structural formula Ig:



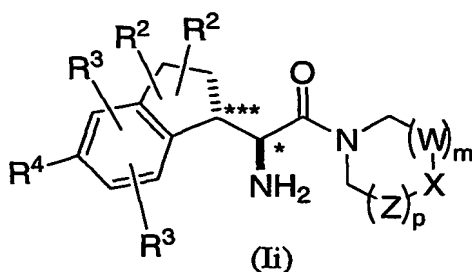
wherein q is 1; R^2 and R^3 are each independently hydrogen or fluorine; and W, X, Z, m, p, and R^4 are as defined in Claim 1.

10. The compound of Claim 9 wherein the carbon atom marked with an * has the stereochemical configuration as depicted in the formula Ih:



5 wherein R² and R³ are each independently hydrogen or fluorine, and W, X, Z, m, p, and R⁴ are as defined in Claim 1.

11. The compound of Claim 9 wherein the carbon atom marked with an * and the carbon atom marked with an *** have the stereochemical configurations as depicted in the
10 formula Ii:



wherein R² and R³ are each independently hydrogen or fluorine, and W, X, Z, m, p, and R⁴ are as defined in Claim 1.

15 12. The compound of Claim 11 wherein X is CH₂, S, CHF, or CF₂;
W and Z are each independently CH₂, CHF, or CF₂;
R⁴ is hydrogen, halogen, phenyl, heteroaryl, or heterocyclyl, wherein phenyl, heteroaryl, and heterocyclyl are unsubstituted or substituted with one to three R⁵ substituents; and
each R⁵ is independently selected from the group consisting of:
20 halogen,
cyano,
oxo,
hydroxy,

C₁₋₆ alkyl, wherein alkyl is unsubstituted or substituted with one to five halogens,
C₁₋₆ alkoxy, wherein alkoxy is unsubstituted or substituted with one to five halogens,
NR⁶R⁷,
CONR⁶R⁷,
5 OCONR⁶R⁷,
SO₂NR⁶R⁷,
SO₂R⁹,
NR⁸SO₂R⁹,
NR⁸CONR⁶R⁷,
10 NR⁸COR⁸,
NR⁸CO₂R⁹,
COOH,
COOC₁₋₆ alkyl,

15 aryl, wherein aryl is unsubstituted or substituted with one to five substituents
independently selected from halogen, hydroxy, CO₂H, C₁₋₆ alkyloxycarbonyl,
C₁₋₆ alkyl, and C₁₋₆ alkoxy, wherein alkyl and alkoxy are unsubstituted or
substituted with one to five halogens,

heteroaryl, wherein heteroaryl is unsubstituted or substituted with one to three
20 substituents independently selected from hydroxy, halogen, CO₂H,
C₁₋₆ alkyloxycarbonyl, C₁₋₆ alkyl, and C₁₋₆ alkoxy, wherein alkyl and alkoxy
are unsubstituted or substituted with one to five halogens,

heterocyclyl, wherein heterocyclyl is unsubstituted or substituted with one to three
substituents independently selected from oxo, hydroxy, halogen, CO₂H,
C₁₋₆ alkyloxycarbonyl, C₁₋₆ alkyl, and C₁₋₆ alkoxy, wherein alkyl and alkoxy
25 are unsubstituted or substituted with one to five halogens, and

(CH₂)_n-C₃₋₆ cycloalkyl, wherein cycloalkyl is unsubstituted or substituted with one to
three substituents independently selected from halogen, hydroxy, C₁₋₆ alkyl, and
C₁₋₆ alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one
30 to five halogens.

13. The compound of Claim 12 wherein each R⁵ is independently selected
from the group consisting of:

halogen,

oxo,

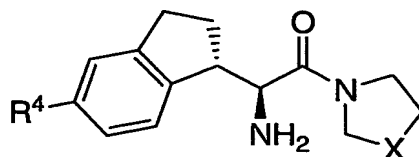
35 C₁₋₆ alkyl, wherein alkyl is unsubstituted or substituted with one to five halogens,

C₁₋₆ alkoxy, wherein alkoxy is unsubstituted or substituted with one to five halogens,
and
C₃₋₆ cycloalkyl.

14. The compound of Claim 12 wherein R⁴ is selected from the group consisting of:

hydrogen,
bromo,
4-fluorophenyl,
2-methoxyphenyl,
1-methylpiperidin-2-on-5-yl,
1-methylpyridin-2(1H)-on-5-yl,
[1,2,4]triazolo[4,3-*a*]pyridin-6-yl,
3-(cyclopropyl)[1,2,4]triazolo[4,3-*a*]pyridin-6-yl,
[1,2,4]triazolo[1,5-*a*]pyridin-6-yl,
[1,2,4]triazolo[1,5-*a*]pyridin-7-yl,
[1,2,4]triazolo[1,5-*a*]pyrazin-5-yl,
2-(trifluoromethyl)[1,2,4]triazolo[1,5-*a*]pyrazin-5-yl, and
1-methylpyrimidin-2(1*H*)-on-5-yl.

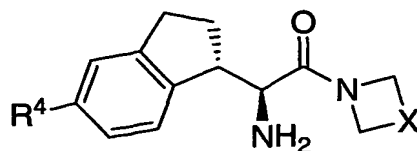
15. The compound of Claim 14 of the structural formula selected from the group consisting of:



<u>R⁴</u>	<u>X</u>
H	(<i>S</i>)-CHF
Br	(<i>S</i>)-CHF
4-F-Ph	(<i>S</i>)-CHF
2-OMe-Ph	(<i>S</i>)-CHF

1-methylpyridin-2(1 <i>H</i>)-on-5-yl	(<i>S</i>)-CHF
1-methyl-piperidin-2-on-5-yl	(<i>S</i>)-CHF
[1,2,4]triazolo[1,5- <i>a</i>]pyridin-6-yl	(<i>S</i>)-CHF
[1,2,4]triazolo[4,3- <i>a</i>]pyridin-6-yl	(<i>S</i>)-CHF
3-Cyclopropyl[1,2,4]triazolo[4,3- <i>a</i>]pyridin-6-yl	(<i>S</i>)-CHF
Br	CF ₂
2-(trifluoromethyl)- [1,2,4]triazolo[1,5- <i>a</i>]pyrazin-5-yl	(<i>S</i>)-CHF
[1,2,4]triazolo[1,5- <i>a</i>]pyrazin-5-yl	(<i>S</i>)-CHF
1-methylpyridin-2(1 <i>H</i>)-on-5-yl	CF ₂
2-(trifluoromethyl)- [1,2,4]triazolo[1,5- <i>a</i>]pyrazin-5-yl	CF ₂
[1,2,4]triazolo[1,5- <i>a</i>]pyrazin-5-yl	CF ₂
1-methylpiperidin-2-on-5-yl	CF ₂
1-methylpyrimidin-2(1 <i>H</i>)-on-5-yl	(<i>S</i>)-CHF

16. The compound of Claim 14 of the structural formula selected from the group consisting of:



<u>R⁴</u>	<u>X</u>
Br	CHF
4-F-Ph	CHF
1-methylpyridin-2(1 <i>H</i>)-on-5-yl	CHF
[1,2,4]triazolo[4,3- <i>a</i>]pyridin-6-yl	CHF
[1,2,4]triazolo[1,5- <i>a</i>]pyridin-6-yl	CHF
[1,2,4]triazolo[1,5- <i>a</i>]pyrazin-5-yl	CHF
2-(trifluoromethyl)- [1,2,4]triazolo[1,5- <i>a</i>]pyrazin-5-yl	CHF
2-methyl-1,4-dihydro-isoquinolin- 3(2 <i>H</i>)-on-7-yl	CHF
1-methylpiperidin-2-on-5-yl	CHF
1-methylpyrimidin-2(1 <i>H</i>)-on-5-yl	CHF

17. A pharmaceutical composition which comprises a compound of Claim 1 and a pharmaceutically acceptable carrier.

5

18. A method for inhibiting dipeptidyl peptidase-IV enzyme activity in a mammal in need thereof which comprises the administration to the mammal of an effective amount of a compound of Claim 1.

19. A method for treating diabetes in a mammal in need thereof which comprises the administration to the mammal of a therapeutically effective amount of a compound of Claim 1.

5 20. A method for treating non-insulin dependent (Type 2) diabetes in a mammal in need thereof which comprises the administration to the mammal of a therapeutically effective amount of a compound of Claim 1.

10 21. A method for treating hyperglycemia in a mammal in need thereof which comprises the administration to the mammal of a therapeutically effective amount of a compound of Claim 1.

15 22. A method for treating obesity in a mammal in need thereof which comprises the administration to the mammal of a therapeutically effective amount of a compound of Claim 1.

20 23. A method for treating one or more lipid disorders selected from the group of dyslipidemia, hyperlipidemia, hypertriglyceridemia, hypercholesterolemia, low HDL and high LDL in a mammal in need thereof which comprises the administration to the mammal of a therapeutically effective amount of a compound of Claim 1.

24. A method for treating in a mammal in need thereof one or more conditions selected from the group consisting of (1) hyperglycemia, (2) low glucose tolerance, (3) insulin resistance, (4) obesity, (5) lipid disorders, (6) dyslipidemia, (7) hyperlipidemia, (8) hypertriglyceridemia, (9) hypercholesterolemia, (10) low HDL levels, (11) high LDL levels, (12) atherosclerosis and its sequelae, (13) vascular restenosis, (14) irritable bowel syndrome, (15) inflammatory bowel disease, including Crohn's disease and ulcerative colitis, (16) other inflammatory conditions, (17) pancreatitis, (18) abdominal obesity, (19) neurodegenerative disease, (20) retinopathy, (21) nephropathy, (22) neuropathy, (23) Syndrome X, (24) ovarian hyperandrogenism (polycystic ovarian syndrome), and other disorders where insulin resistance is a component, wherein the method comprises the administration to the mammal a therapeutically effective amount of a compound of Claim 1.

25. The pharmaceutical composition of Claim 17 further comprising one or more additional active ingredients selected from the group consisting of:

(a) a second dipeptidyl peptidase IV inhibitor;

(b) an insulin sensitizer selected from the group consisting of a PPAR γ agonist, a PPAR α/γ dual agonist, a PPAR α agonist, a biguanide, and a protein tyrosine phosphatase-1B inhibitor;

5 (c) an insulin or insulin mimetic;

(d) a sulfonylurea or other insulin secretagogue;

(e) an α -glucosidase inhibitor;

(f) a glucagon receptor antagonist;

(g) GLP-1, a GLP-1 mimetic, or a GLP-1 receptor agonist;

10 (h) GIP, a GIP mimetic, or a GIP receptor agonist;

(i) PACAP, a PACAP mimetic, or a PACAP receptor agonist;

(j) a cholesterol lowering agent such as (i) HMG-CoA reductase inhibitor, (ii) sequestrant, (iii) nicotinic alcohol, nicotinic acid or a salt thereof, (iv) PPAR α agonist, (v) PPAR α/γ dual agonist, (vi) inhibitor of cholesterol absorption, (vii) acyl CoA:cholesterol
15 acyltransferase inhibitor, and (viii) anti-oxidant;

(k) a PPAR δ agonist;

(l) an antiobesity compound;

(m) an ileal bile acid transporter inhibitor;

(n) an anti-inflammatory agent;

20 (o) an antihypertensive agent; and

(p) an activator of glucokinase.

26. The pharmaceutical composition of Claim 25 wherein the PPAR α/γ dual agonist is KRP-297.

25 27. A method of treating diabetes in a mammal in need thereof comprising administering to the mammal a therapeutically effective amount of a compound of Claim 1 in combination with the PPAR α/γ dual agonist KRP-297.